```
=> d que stat l79
L78           1 SEA FILE=REGISTRY ABB=ON  76555-98-1/RN
L79           7 SEA FILE=HCAPLUS ABB=ON  L78

=> d ibib abs hitstr l79 1-7

L79  ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2001:748108  HCAPLUS
DOCUMENT NUMBER:          135:300482
TITLE:                    Isolation of functionally active γ-secretase
                          presenilin 1 complex and fluorescence assay for
                          γ-secretase activity and inhibitors
INVENTOR(S):              Roberts, Susan B.; Hendrick, Joseph P.; Vinitsky,
                          Alexander; Lewis, Martin; Smith, David W.; Pak, Roger
PATENT ASSIGNEE(S):       Bristol-Myers Squibb Company, USA
SOURCE:                   PCT Int. Appl., 127 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    ---------------------    --------
     WO 2001075435         A2    20011011    WO 2001-US10453          20010330
     WO 2001075435         A3    20020808
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2405332            AA    20011011    CA 2001-2405332          20010330
     US 2002025540         A1    20020228    US 2001-823153           20010330
     US 6713248            B2    20040330
     EP 1305634            A2    20030502    EP 2001-922976           20010330
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004505608         T2    20040226    JP 2001-572863           20010330
     US 2004121411         A1    20040624    US 2003-713981           20031114
PRIORITY APPLN. INFO.:                       US 2000-194495P      P   20000403
                                             US 2001-823153       A3  20010330
                                             WO 2001-US10453      W   20010330
AB   The present invention provides an isolated, functionally-active protein
     that catalyzes cleavage of a γ-secretase substrate. The functional
     activity of the isolated protein suggests that the isolated protein
     includes γ-secretase. In one embodiment, the isolated
     γ-secretase protein is associated with presenilin 1. The present
     invention also relates to homogeneous methods for monitoring cleavage of
     β-amyloid precursor protein (βAPP) by γ-secretase, wherein
     the steps of isolating and retrieving cleavage products have been
     eliminated. Cleavage can be detected by binding a pair of fluorescent
     adducts to the γ-cleaved βAPP fragment. Preferably, a first
     fluorescent adduct binds to the carboxy-terminal end of the
     γ-cleaved βAPP fragment, with substantially no cross-reactivity
     to uncleaved βAPP or to other types of γ-cleaved βAPP
     fragments, while a second fluorescent adduct binds to a portion within the
```

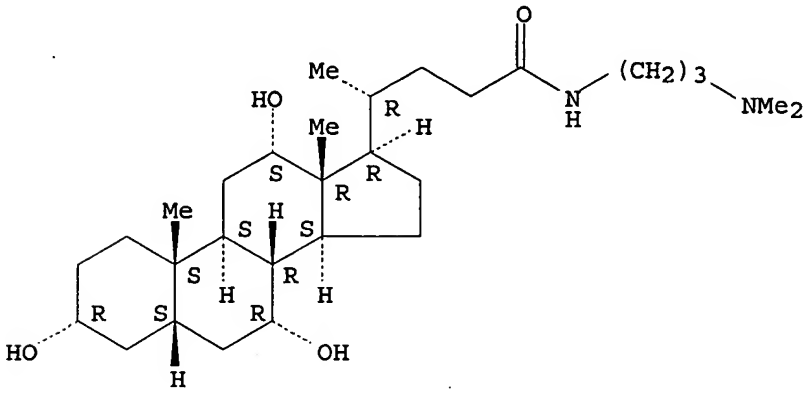
amino-terminal region on the γ-cleaved βAPP fragment. Detection of binding to the γ-cleaved βAPP fragment is determined by monitoring the fluorescent energy transfer between the adducts.

IT **76555-98-1**
RL: NUU (Other use, unclassified); USES (Uses)
(solubilizer; isolation of functionally active γ-secretase presenilin 1 complex and fluorescence assay for γ-secretase activity and inhibitors)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:75714 HCAPLUS
DOCUMENT NUMBER: 108:75714
TITLE: Steroids and their cyclic hydrocarbon analogs with amino-containing sidechains, useful as antidiabetic agents and inhibitors of phospholipase A2
INVENTOR(S): Johnson, Roy A.; Bundy, Gordon L.; Youngdale, Gilbert A.; Morton, Douglas R.
PATENT ASSIGNEE(S): Upjohn Co. , USA
SOURCE: PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8702367	A2	19870423	WO 1986-US2116	19861007
WO 8702367	A3	19880630		
W: JP, US, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
EP 243449	A1	19871104	EP 1986-906569	19861007
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 63501217	T2	19880512	JP 1986-505710	19861007
US 4917826	A	19900417	US 1987-117851	19870616
US 5196542	A	19930323	US 1991-657721	19910220
US 5145874	A	19920908	US 1991-663037	19910225
US 5187299	A	19930216	US 1991-793486	19911113

US 5274089	A	19931228	US 1992-972693	19921106
US 5334712	A	19940802	US 1992-976751	19921116
US 5373095	A	19941213	US 1993-126153	19930923
US 5621123	A	19970415	US 1994-247169	19940520
PRIORITY APPLN. INFO.:			US 1985-788995	A2 19851018
			US 1986-843120	A2 19860324
			WO 1986-US2116	W 19861007
			US 1987-117851	A3 19870616
			US 1989-394396	A3 19890815
			US 1991-657721	A3 19910220
			US 1991-657729	B1 19910220
			US 1991-793486	A3 19911113
			US 1992-972693	A3 19921106
			US 1992-976751	A3 19921116

OTHER SOURCE(S): CASREACT 108:75714

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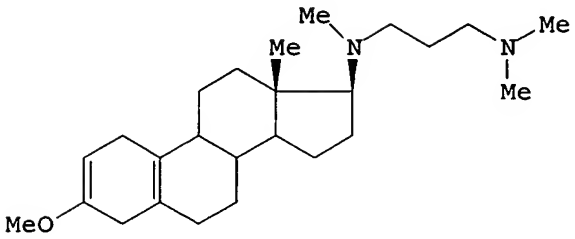


I

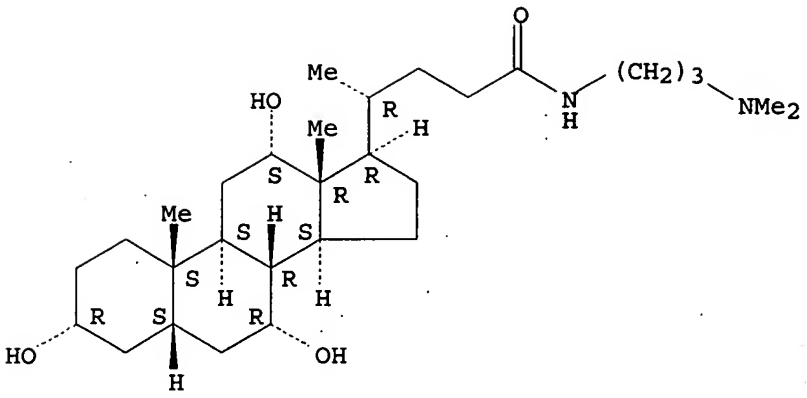
AB A wide variety of steroids and nonsteroidal analogs bearing amino-containing sidechains were prepared for use as antidiabetic agents and in the treatment or prevention of phospholipase A2-mediated conditions. Reductive amination of estrone Me ether with Me2N(CH2)3NH2 and HCO2H at 160-170° gave N-[3-(dimethylamino)propyl]-N-formyl-3-methoxyestra-1,3,5(10)-trien-17β-amine, which was reduced by LiAlH4 in dioxane to the N-Me derivative This underwent Birch reduction, followed by 3 recrystns. in Et2O-MeCN, to give estradienamine derivative I. In the perfused guinea pig lung, I completely inhibited phospholipase A2 at 4 + 10-7 M.

IT **76555-98-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in synthesis of phospholipase A2-inhibiting amino steroids and analogs)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:187118 HCAPLUS
DOCUMENT NUMBER: 104:187118
TITLE: Fixed steroids
INVENTOR(S): Itagaki, Koji; Ito, Takeshi; Ando, Kyoto
PATENT ASSIGNEE(S): Mitsubishi Chemical Industries Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

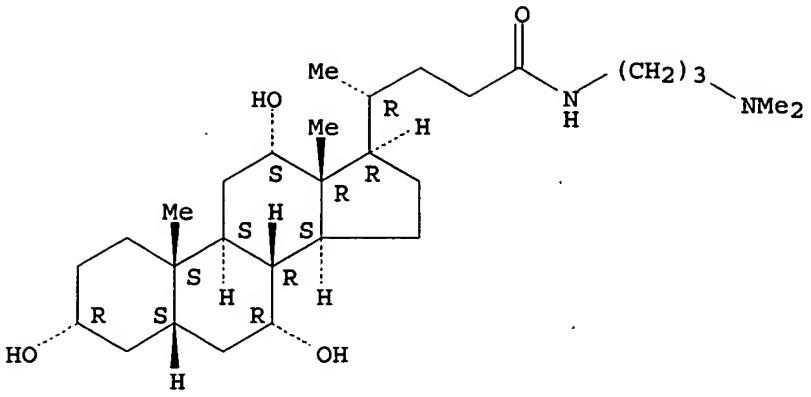
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60133005	A2	19850716	JP 1983-241342	19831221
PRIORITY APPLN. INFO.:			JP 1983-241342	19831221

AB Products useful as carriers in affinity chromatog. are prepared by amidation of carboxylated steroids with polyalkylenepolyamines and reaction of the amides with insol. matrix polymers having amine-reactive groups. Thus, heating 20 g Et cholate with 100 g Me2N(CH2)3NH2 16 h at 140° gave 21.1 g amide. Heating 19.4 g amide and 5 g chloromethylated styrene-divinylbenzene polymer in 1:1 dioxane-MeOH for 16 h at 70° gave 10.3 g fixed steroid (ion exchange volume 1.08 mequiv/g dry resin).

IT **76555-98-1D**, reaction products with chloromethylated styrene copolymers
RL: USES (Uses)
(carriers in affinity chromatog.)

RN 76555-98-1 HCAPLUS
CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



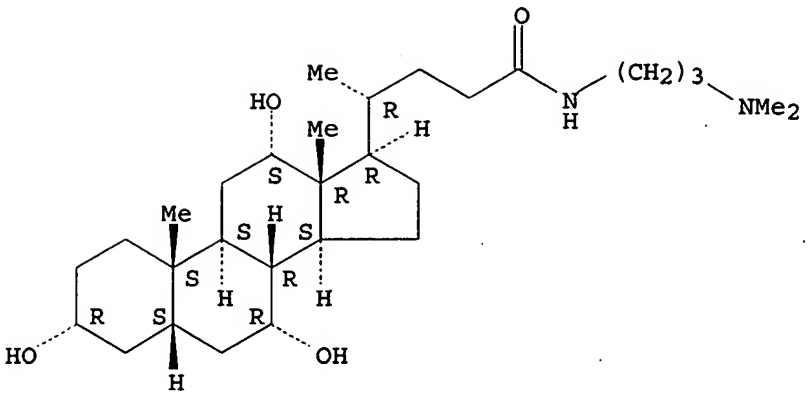
L79 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:402687 HCAPLUS
DOCUMENT NUMBER: 99:2687
TITLE: Sulfobetaine derivatives of bile acids: nondenaturing surfactants for membrane biochemistry
AUTHOR(S): Hjelmeland, Leonard M.; Nebert, Daniel W.; Osborne, James C., Jr.
CORPORATE SOURCE: Dev. Pharmacol. Branch, Natl. Inst. Child Health Hum. Dev., Bethesda, MD, 20205, USA
SOURCE: Analytical Biochemistry (1983), 130(1), 72-82
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The syntheses of 4 new sulfobetaine derivs. of bile salts are presented, along with a general set of criteria for useful detergents in membrane biochem. Phys. properties including the critical micelle concentration, aggregation number, partial sp. volume, critical micellar temperature, UV-visible spectrum, and CD spectrum were examined for the new compds. To examine the interaction of this class of compds. with macromols., CHAPS was further studied. CD spectra of apolipoprotein C-III2 were measured in the presence of varying concns. of CHAPS to determine the effect of this compound on secondary structure.

Gel-exclusion chromatog. and sedimentation equilibrium studies of cytochrome P 450 in the presence of CHAPS was also performed to establish the ability of this detergent to disaggregate cytochrome P 450 to a monomeric/dimeric state.

IT **76555-98-1P**
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(preparation and alkylation of)
RN 76555-98-1 HCAPLUS
CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:452173 HCAPLUS
DOCUMENT NUMBER: 97:52173
TITLE: Nondenaturing zwitterionic detergents for membrane biochemistry
INVENTOR(S): Hjelmeland, Leonard
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U. S. Pat. Appl., 47 pp. Avail. NTIS Order No. PAT-APPL-6-294 203
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

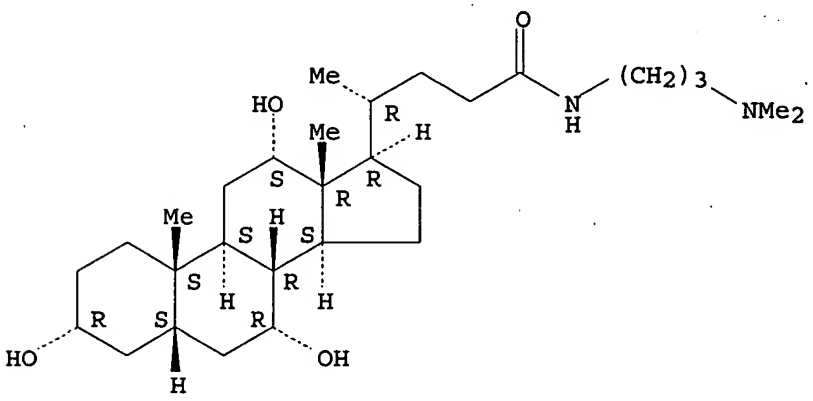
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 294203	A0	19820409	US 1981-294203		19810819
US 4372888	A	19830208			
US 181465	A0	19810327	US 1980-181465		19800826
WO 8300694	A1	19830303	WO 1982-US1123		19820819
W: JP					
RW: AT, BE, CH, DE, FR, GB, LU, NL, SE					
JP 58501279	T2	19830804	JP 1982-502842		19820819
EP 85717	A1	19830817	EP 1982-902934		19820819
EP 85717	B1	19861029			
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE					
CA 1179326	A1	19841211	CA 1982-409779		19820819
AT 23166	E	19861115	AT 1982-902934		19820819
PRIORITY APPLN. INFO.:			US 1980-181465		19800826
			US 1981-294203	A	19810819
			EP 1982-902934	A	19820819
			WO 1982-US1123	W	19820819

AB Preparation of 2 nondenaturing zwitterionic detergents, 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate (CHAPS) and 3-[(3-cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate (CHAPSO), is described for solubilization of membrane proteins. CHAPSO was 2-fold more effective in solubilizing active opiate receptors than CHAPS.

IT **76555-98-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reactions of, with propanesultone or sodium chlorohydroxypropanesulfonate)
RN 76555-98-1 HCAPLUS
CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:438693 HCAPLUS
DOCUMENT NUMBER: 95:38693
TITLE: Nondenaturing zwitterionic detergents for membrane biochemistry
INVENTOR(S): Hjelmeland, Leonard M.
PATENT ASSIGNEE(S): United States Dept. of Health, Education, and Welfare, USA
SOURCE: U. S. Pat. Appl., 22 pp. Avail. NTIS Order No. PAT-APPL-181 465.
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 181465	A0	19810327	US 1980-181465	19800826
CA 1173823	A1	19840904	CA 1981-382720	19810728
EP 46523	A1	19820303	EP 1981-106105	19810804
EP 46523	B1	19840725		
R: BE, CH, DE, FR, GB				
US 294203	A0	19820409	US 1981-294203	19810819
US 4372888	A	19830208		
JP 57073095	A2	19820507	JP 1981-132668	19810826
JP 03002877	B4	19910117		

PRIORITY APPLN. INFO.: US 1980-181465 A 19800826
AB Preparation of zwitterionic detergents, which are a combination of a bile salt hydrophobic group and a sulfobetaine-type polar group, is described for solubilizing membrane proteins in a nondenatured state. 3-[(3-Cholamidopropyl)dimethylammonio]-1-propanesulfonate (I) preparation is described. The Et3NH+ salt of cholic acid was formed in THF, then ethylchloroformate was added to precipitate Et3NHCl, which was removed from the mixed anhydride by filtration. The mixed anhydride reacted with

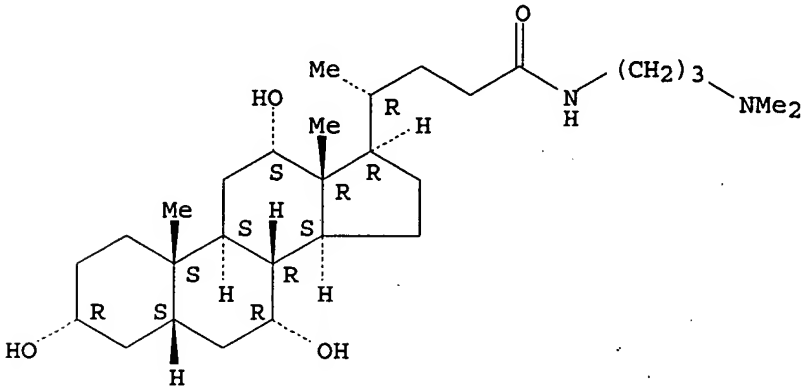
3-dimethylaminopropylamine to form N-(3-dimethylaminopropyl)cholamide (II), EtOH, and CO2. In the final step, the tertiary amine group of II reacted with propane sultone to give the sulfobetaine, I. The yield was 75-80% theor., and the purity of I was >95% as judged by TLC.

IT **76555-98-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with propanesultone)

RN 76555-98-1 HCAPLUS

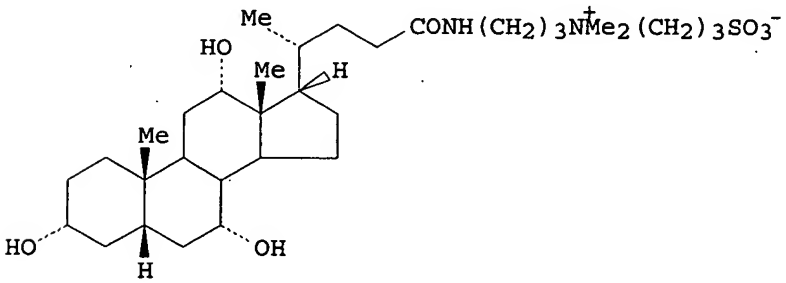
CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1981:79812 HCAPLUS
DOCUMENT NUMBER: 94:79812
TITLE: A nondenaturing zwitterionic detergent for membrane biochemistry: Design and synthesis
AUTHOR(S): Hjelmeland, Leonard M.
CORPORATE SOURCE: Dev. Pharmacol. Branch, Natl. Inst. Child Health Hum. Dev., Bethesda, MD, 20205, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1980), 77(11), 6368-70
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

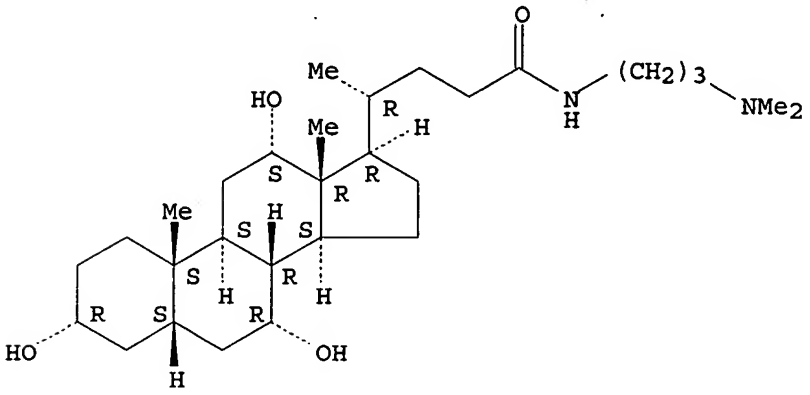
AB The synthesis and evaluation of a new detergent that is a zwitterionic derivative (I) of cholic acid is presented. This detergent combines the useful properties of both the sulfobetaine-type detergents and the bile salt anions. The new detergent proved to be effective at solubilizing membrane proteins in a nondenatured state.

IT **76555-98-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with propanesultone)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Christopher Nichols 10/713981

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DICTIONARY FILE UPDATES:  20 MAR 2005  HIGHEST RN 845957-95-1

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*                                                                   *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                   *
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Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> e mchapso/cn 5
E1            1     MCH90/CN
E2            1     MCHA-1A4/CN
E3            0 --> MCHAPSO/CN
E4            1     MCHB PROTEIN (ESCHERICHIA COLI CFT073 STRAIN CFT073 GENE MCH
                    B)/CN
E5            1     MCHC PROTEIN (ESCHERICHIA COLI CFT073 STRAIN CFT073 GENE MCH
                    C)/CN

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cholan-2-amide"/cn
E1            1     N-(3'-SULFOPHENYL)ANTHRANILIC ACID/CN
E2            1     N-(3'-TRIFLUOROMETHYL-6'-CARBOXYPHENYL)ANTHRANILIC ACID/CN
E3            0 --> N-(3(DIMETHYLAMINO)PROPRYL)3,7,12-TRIHYDROXY(3A, 5B, 7A, 12A
                    ) CHOLAN-2-AMIDE/CN
E4            1     N-(3(R)-(4-CHLOROPHENYL)-1(S)-METHYL-2(S)-PHENYLBUTYL)-2-((3
                    ,5-DIFLUORO-4-METHYLPHENYL)OXY)-2-METHYLPROPANAMIDE/CN
E5            1     N-(3(S)-(4-CHLOROPHENYL)-1(S)-METHYL-2(S)-PHENYLBUTYL)-2-((3
                    ,5-DIFLUORO-4-METHYLPHENYL)OXY)-2-METHYLPROPANAMIDE/CN
E6            1     N-(3(TERT-BUTOXYCARBONYLAMINO)PROPYL)-1-DEOXYNOJIRIMYCIN/CN
E7            1     N-(3)-METHYL-N-(5)-ETHYL-N-(5)-MONOHYDROLUMIFLAVIN/CN
E8            1     N-(3,3,3-TRIFLUOROETHYL)NORAPOMORPHINE/CN
E9            1     N-(3,3,3-TRIFLUOROETHYL)NORAPOMORPHINE HYDROBROMIDE/CN
E10           1     N-(3,3,3-TRIFLUOROETHYL)NORAPOMORPHINE HYDROCHLORIDE/CN
E11           1     N-(3,3,3-TRIFLUOROPROPYL)-1H-INDAZOLE-5-CARBOXAMIDE/CN
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Searched by: Mary Hale 571-272-2507 REM 1D86

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E12             1      N-(3,3,3-TRIFLUOROPROPYL)-N-((2,3-DICHLOROPHENYL)METHYL)PIPE
                       RIDIN-4-AMINE FUMARATE/CN

=> s dimethylamino(l)propyl(l)trihydroxy(l)cholan(l)amide
        462857 DIMETHYLAMINO
       2149448 PROPYL
             4 PROPYLS
       2149448 PROPYL
                 (PROPYL OR PROPYLS)
         73372 TRIHYDROXY
         16504 CHOLAN
       3410082 AMIDE
          1031 AMIDES
       3410082 AMIDE
                 (AMIDE OR AMIDES)
L1             4 DIMETHYLAMINO(L)PROPYL(L)TRIHYDROXY(L)CHOLAN(L)AMIDE

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                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  24.29      24.50

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FILE COVERS 1907 - 22 Mar 2005  VOL 142 ISS 13
FILE LAST UPDATED: 21 Mar 2005  (20050321/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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         68456 DIMETHYLAMINO
             1 DIMETHYLAMINOS
         68457 DIMETHYLAMINO
                 (DIMETHYLAMINO OR DIMETHYLAMINOS)
         84608 PROPYL
             5 PROPYLS
         84611 PROPYL
                 (PROPYL OR PROPYLS)
        146526 PR
          1802 PRS
        147678 PR
                 (PR OR PRS)
        217114 PROPYL
                 (PROPYL OR PR)
         18811 TRIHYDROXY
```

Searched by: Mary Hale 571-272-2507 REM 1D86

```
            568 CHOLAN
         118292 AMIDE
          74906 AMIDES
         161409 AMIDE
                (AMIDE OR AMIDES)
              0 DIMETHYLAMINO(L)PROPYL(L)TRIHYDROXY(L)CHOLAN(L)AMIDE
              0 MCHAPSO
L2            9 L1 OR DIMETHYLAMINO(L)PROPYL(L)TRIHYDROXY(L)CHOLAN(L)AMIDE OR
                MCHAPSO

=> d 1-9 cbib abs hitstr
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Searched by: Mary Hale 571-272-2507 REM 1D86

L2 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

2001:748108 Document No. 135:300482 Isolation of functionally active γ-secretase presenilin 1 complex and fluorescence assay for γ-secretase activity and inhibitors. Roberts, Susan B.; Hendrick, Joseph P.; Vinitsky, Alexander; Lewis, Martin; Smith, David W.; Pak, Roger

(Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2001075435 A2 20011011, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US10453 20010330. PRIORITY: US 2000-PV194495 20000403.

AB The present invention provides an isolated, functionally-active protein that catalyzes cleavage of a γ-secretase substrate. The functional activity of the isolated protein suggests that the isolated protein includes γ-secretase. In one embodiment, the isolated γ-secretase protein is associated with presenilin 1. The present invention also relates to homogeneous methods for monitoring cleavage of β-amyloid precursor protein (βAPP) by γ-secretase, wherein the steps of isolating and retrieving cleavage products have been eliminated. Cleavage can be detected by binding a pair of fluorescent adducts to the γ-cleaved βAPP fragment. Preferably, a first fluorescent adduct binds to the carboxy-terminal end of the γ-cleaved βAPP fragment, with substantially no cross-reactivity to uncleaved βAPP or to other types of γ-cleaved βAPP fragments, while a second fluorescent adduct binds to a portion within the amino-terminal region on the γ-cleaved βAPP fragment. Detection of binding to the γ-cleaved βAPP fragment is determined by monitoring the fluorescent energy transfer between the adducts.

IT 76555-98-1

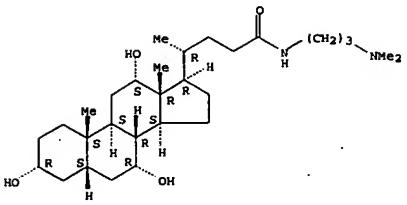
RL: NUU (Other use, unclassified); USES (Uses)
(solubilizer; isolation of functionally active γ-secretase presenilin 1 complex and fluorescence assay for γ-secretase activity and inhibitors)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L2 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L2 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

1997:21100 Document No. 126:75132 Design and Synthesis of Molecular Umbrellas. Janout, Vaclav; Lanier, Marion; Regen, Steven L. (Department of Chemistry, Lehigh University, Bethlehem, PA, 18015, USA). Journal of the American Chemical Society, 119(4), 640-647 (English) 1997. CODEN: JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.

AB The design and synthesis of a series of conjugates derived from cholic acid, spermidine, and 5-(dimethylamino)-1-naphthalenesulfonyl (dansyl), which effectively shield the dansyl moiety from water is described. Direct coupling of cholic acid to both terminal amino groups of spermidine, and attachment of the environmentally-sensitive dansyl moiety to the remaining secondary amine, yields a mol. umbrella (I) whose fluorescent properties (λmax and emission intensity) reflect a nonpolar microenvironment in water and one that is relatively polar in intermediate dimethoxyethane/water mixts. Comparison of I with analogous single-walled and no-walled umbrellas further indicates that a min. of two walls is necessary in order to have umbrella-like properties. Examination of the fluorescent properties of a related double-walled umbrella, bearing a flexible (2-hydroxyethyl)carbamate moiety at the C-3 position of the sterol, reveals that umbrella-like properties are present even when facial amphiphilicity is not rigorously maintained; however, the mol.'s ability to shield the fluorophore, as judged by its relative emission intensity, is diminished. Methyl-capping of the (2-hydroxyethyl)carbamate enhances the umbrella's ability to provide a hydrophobic shelter in water. A tetra-walled analog of I, bearing four cholic acid units, has been synthesized and its dansyl group has reduced exposure toward water. The potential utility of mol. umbrellas in the area of drug delivery is briefly discussed.

IT 185450-86-6P 185450-89-9P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of surfactant dansylaminoacetylbischolylspermidine derivs.)

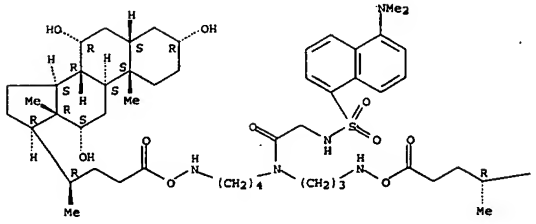
RN 185450-86-6 HCAPLUS

CN Acetamide, 2-[[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]amino]-N-[4-[[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]oxy]amino]butyl]-N-[3-[[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]oxy]amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L2 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-A



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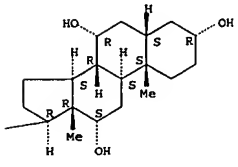


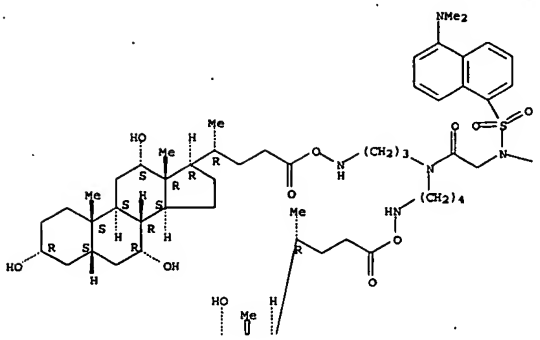
RN 185450-89-9 HCAPLUS

CN Acetamide, 2,2'-[[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]imino]bis[N-[4-[[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]oxy]amino]butyl]-N-[3-[[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]oxy]amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L2 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-A



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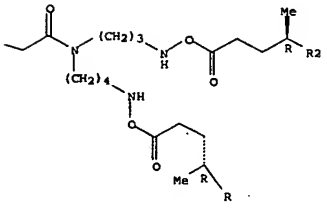
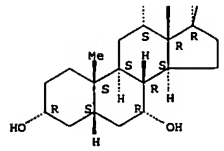


L2 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 2-A



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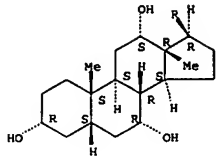

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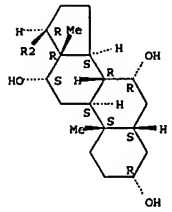


L2 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

1996:62571 Document No. 124:185506 Molecular umbrellas. Janout, Vaclav; Lanier, Marion; Regen, Steven L. (Department of Chemistry, Lehigh University, Bethlehem, PA, 18015, USA). Journal of the American Chemical Society, 118(6), 1573-4 (English) 1996. CODEN: JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.

AB In this paper, a new concept in surfactant chemical is introduced that is based on mols. that mimic the structure and function of umbrellas; i.e., mols. that can cover an attached agent and shield it from an incompatible environment. A prototype "double-walled" umbrella has been synthesized using cholic acid as "wall material", spermidine as a scaffold, and an environmentally-sensitive, fluorescent probe, 5-dimethylamino-1-naphthalene sulfonyl (Dansyl) as the agent. Fluorescence measurements carried out in varying mixts. of dimethoxyethane/water reveal a "turning point"; i.e., a DME/water ratio at which a min. fluorescence intensity is observed In striking contrast, a single-walled analog and a control mol. do not exhibit a turning point; in these latter cases, the fluorescence continuously decreases as the water content increases. Potential applications of this new class of compds. in the areas of drug design and drug delivery are briefly discussed.

IT 174094-97-4P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(mol. umbrellas for drug delivery)

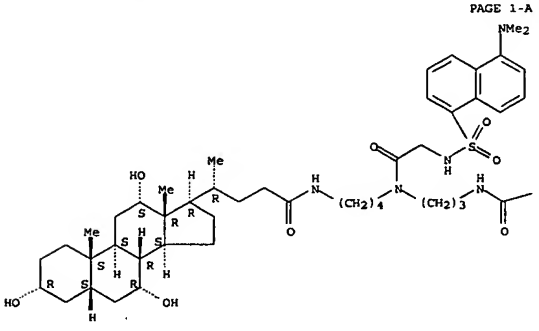
RN 174094-97-4 HCAPLUS

CN Cholan-24-amide, N-[3-[[[[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]amino]acetyl][4-[[(3α,5β,7α,12.alph

a.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]butyl]amino]propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

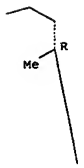
Absolute stereochemistry.

PAGE 1-A



L2 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-B



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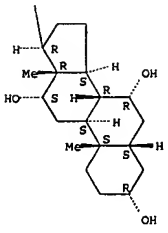
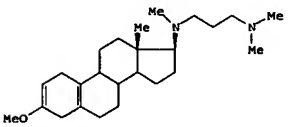


Searched by: Mary Hale 571-272-2507 REM 1D86

L2 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
1988:75714 Document No. 108:75714 Steroids and their cyclic hydrocarbon analogs with amino-containing sidechains, useful as antidiabetic agents and inhibitors of phospholipase A2. Johnson, Roy A.; Bundy, Gordon L.; Youngdale, Gilbert A.; Morton, Douglas R. (Upjohn Co. , USA). PCT Int. Appl. WO 8702367 A2 19870423, 177 pp. DESIGNATED STATES: W: JP, US, US; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1986-US2116 19861007. PRIORITY: US 1985-788995 19851018; US 1986-843120 19860324.

GI



I

AB A wide variety of steroids and nonsteroidal analogs bearing amino-containing sidechains were prepared for use as antidiabetic agents and in the treatment or prevention of phospholipase A2-mediated conditions. Reductive amination of estrone Me ether with Me2N(CH2)3NH2 and HCO2H at 160-170° gave N-[3-(dimethylamino)propyl]-N-formyl-3-methoxyestra-1,3,5(10)-trien-17β-amine, which was reduced by LiAlH4 in dioxane to the N-Me derivative This underwent Birch reduction, followed by 3 recrystns. in Et2O-MeCN, to give estradienamine derivative I. In the perfused guinea pig lung, I completely inhibited phospholipase A2 at 4 + 10-7 M.

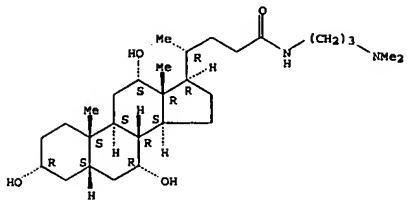
IT 76555-98-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in synthesis of phospholipase A2-inhibiting amino steroids and analogs)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L2 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L2 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
1986:187118 Document No. 104:187118 Fixed steroids. Itagaki, Koji; Ito, Takeshi; Ando, Kyoto (Mitsubishi Chemical Industries Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 60133005 A2 19850716 Showa, 6 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1983-241342 19831221.

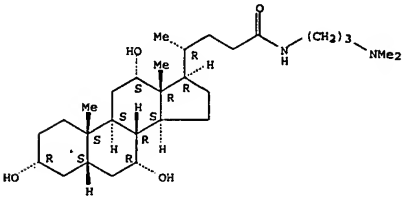
AB Products useful as carriers in affinity chromatog. are prepared by amidation of carboxylated steroids with polyalkylenepolyamines and reaction of the amides with insol. matrix polymers having amine-reactive groups. Thus, heating 20 g Et cholate with 100 g Me2N(CH2)3NH2 16 h at 140° gave 21.1 g amide. Heating 19.4 g amide and 5 g chloromethylated styrene-divinylbenzene polymer in 1:1 dioxane-MeOH for 16 h at 70° gave 10.3 g fixed steroid (ion exchange volume 1.08 mequiv/g dry resin).

IT 76555-98-1D, reaction products with chloromethylated styrene copolymers
RL: USES (Uses)
(carriers in affinity chromatog.)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L2 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
1983:402687 Document No. 99:2687 Sulfobetaine derivatives of bile acids: nondenaturing surfactants for membrane biochemistry. Hjelmeland, Leonard M.; Nebert, Daniel W.; Osborne, James C., Jr. (Dev. Pharmacol. Branch, Natl. Inst. Child Health Hum. Dev., Bethesda, MD, 20205, USA). Analytical Biochemistry, 130(1), 72-82 (English) 1983. CODEN: ANBCA2. ISSN: 0003-2697.

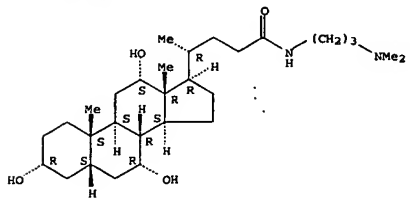
AB The syntheses of 4 new sulfobetaine derivs. of bile salts are presented, along with a general set of criteria for useful detergents in membrane biochem. Phys. properties including the critical micelle concentration, aggregation number, partial sp. volume, critical micellar temperature, UV-visible spectrum, and CD spectrum were examined for the new compds. To examine the interaction of this class of compds. with macromols., CHAPS was further studied. CD spectra of apolipoprotein C-III2 were measured in the presence of varying concns. of CHAPS to determine the effect of this compound on secondary structure. Gel-exclusion chromatog. and sedimentation equilibrium studies of cytochrome P 450 in the presence of CHAPS was also performed to establish the ability of this detergent to disaggregate cytochrome P 450 to a monomeric/dimeric state.

IT 76555-98-1P
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(preparation and alkylation of)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L2 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
1982:452173 Document No. 97:52173 Nondenaturing zwitterionic detergents for membrane biochemistry. Hjelmeland, Leonard (United States Dept. of Health and Human Services, USA). U. S. Pat. Appl. US 294203 A0 19820409, 47 pp. Avail. NTIS Order No. PAT-APPL-6-294 203 (English). CODEN: XAXXAV. APPLICATION: US 1981-294203 19810826.

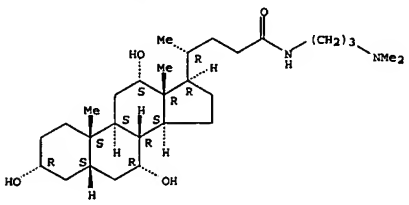
AB Preparation of 2 nondenaturing zwitterionic detergents, 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate (CHAPS) and 3-[(3-cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate (CHAPSO), is described for solubilization of membrane proteins. CHAPSO was 2-fold more effective in solubilizing active opiate receptors than CHAPS.

IT 76555-98-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reactions of, with propanesultone or sodium chlorohydroxypropanesulfonate)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L2 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
1981:438693 Document No. 95:38693 Nondenaturing zwitterionic detergents for membrane biochemistry. Hjelmeland, Leonard M. (United States Dept. of Health, Education, and Welfare, USA). U. S. Pat. Appl. US 181465 19810327, 22 pp. Avail. NTIS Order No. PAT-APPL-181 465. (English). CODEN: XAXXAV. APPLICATION: US 1980-181465 19800826.

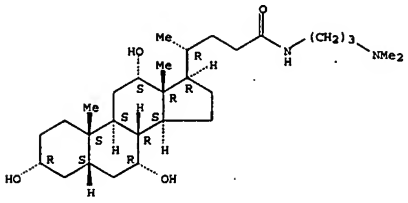
AB Preparation of zwitterionic detergents, which are a combination of a bile salt hydrophobic group and a sulfobetaine-type polar group, is described for solubilizing membrane proteins in a nondenatured state. 3-[(3-Cholamidopropyl)dimethylammonio]-1-propanesulfonate (I) preparation is described. The Et3NH+ salt of cholic acid was formed in THF, then ethylchloroformate was added to precipitate Et3NHCl, which was removed from the mixed anhydride by filtration. The mixed anhydride reacted with 3-dimethylaminopropylamine to form N-(3-dimethylaminopropyl)cholamide (II), EtOH, and CO2. In the final step, the tertiary amine group of II reacted with propane sultone to give the sulfobetaine, I. The yield was 75-80% theor., and the purity of I was >95% as judged by TLC.

IT 76555-98-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with propanesultone)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L2 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
1981:79812 Document No. 94:79812 A nondenaturing zwitterionic detergent for membrane biochemistry: Design and synthesis. Hjelmeland, Leonard M. (Dev. Pharmacol. Branch, Natl. Inst. Child Health Hum. Dev., Bethesda, MD, 20205, USA). Proceedings of the National Academy of Sciences of the United States of America, 77(11), 6368-70 (English) 1980. CODEN: PNASA6. ISSN: 0027-8424.

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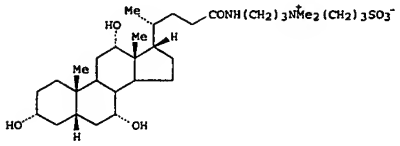


I

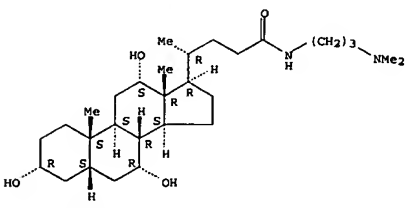
AB The synthesis and evaluation of a new detergent that is a zwitterionic derivative (I) of cholic acid is presented. This detergent combines the useful properties of both the sulfobetaine-type detergents and the bile salt anions. The new detergent proved to be effective at solubilizing membrane proteins in a nondenatured state.

IT 76555-98-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with propanesultone)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Searched by: Mary Hale 571-272-2507 REM 1D86

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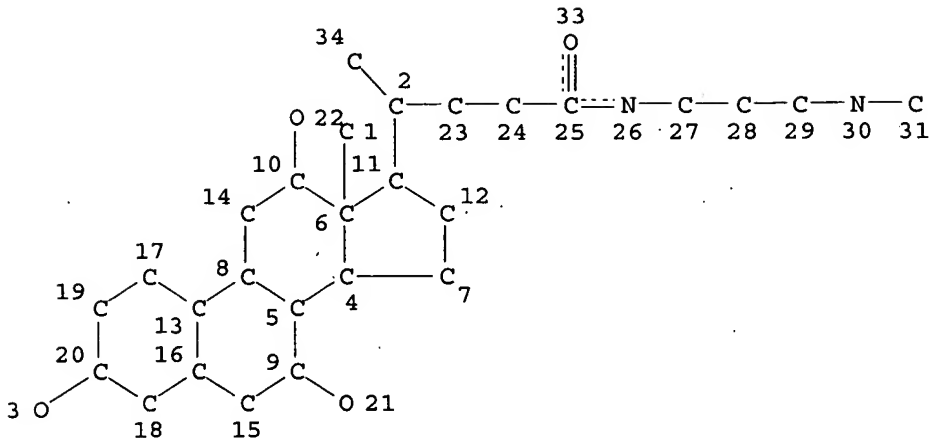

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DEFAULT ECLEVEL IS LIMITED

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-6.57

FILE 'HCAPLUS' ENTERED AT 14:02:07 ON 22 MAR 2005

Searched by: Mary Hale 571-272-2507 REM 1D86

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FILE COVERS 1907 - 22 Mar 2005 VOL 142 ISS 13
FILE LAST UPDATED: 21 Mar 2005 (20050321/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L8 1067 L7

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L15 3 L8 AND (L9 OR L10 OR L11 OR L12 OR L13 OR L14)

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Searched by: Mary Hale 571-272-2507 REM 1D86

L15 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

2002:107078 Document No. 136:166050 Novel methods and compositions to upregulate, redirect or limit immune responses to peptides, proteins and other bioactive compounds and vectors expressing the same. Bot, Adrian; Dellamary, Luis; Smith, Dan J.; Woods, Catherine M. (Alliance Pharmaceutical Corp., USA). PCT Int. Appl. WO 2002009674 A2 20020207, 80 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US24038 20010730. PRIORITY: US 2000-PV221544 20000728.

AB Novel compns. are disclosed which can induce or enhance an immune response against foreign or self antigens (microbial or parasitic) or modulate (suppress) the activity of pathogenic cells in inflammatory or autoimmune diseases. Compns. and methods are taught in how to limit the generation of an immune response against formulated peptides and proteins with application in antibody therapy or hormone replacement therapy. Methods of suppressing autoimmunity are also disclosed which use ligands for cellular receptors expressed on cells of the innate immune system and more specifically for down-regulation of autoimmune processes by either deletion or induction of anergy at the level of autoreactive T cells or by triggering active-suppressor T cells that down-regulate the activity of pathogenic cells.

IT 75621-03-3

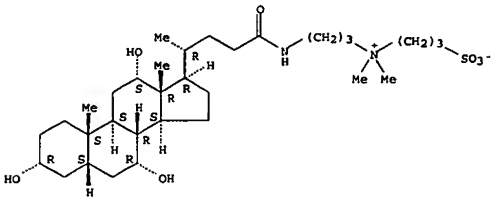
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(novel methods and compns. to modulate and control immune responses and immune disorders)

RN 75621-03-3 HCAPLUS

CN 1-Propanaminium, N,N-dimethyl-N-(3-sulfopropyl)-3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L15 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L15 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

2001:748108 Document No. 135:300482 Isolation of functionally active γ-secretase presenilin 1 complex and fluorescence assay for γ-secretase activity and inhibitors. Roberts, Susan B.; Hendrick, Joseph P.; Vinitsky, Alexander; Lewis, Martin; Smith, David W.; Pak, Roger (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2001075435 A2 20011011, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US10453 20010330. PRIORITY: US 2000-PV194495 20000403.

AB The present invention provides an isolated, functionally-active protein that catalyzes cleavage of a γ-secretase substrate. The functional activity of the isolated protein suggests that the isolated protein includes γ-secretase. In one embodiment, the isolated γ-secretase protein is associated with presenilin 1. The present invention also relates to homogeneous methods for monitoring cleavage of β-amyloid precursor protein (βAPP) by γ-secretase, wherein the steps of isolating and retrieving cleavage products have been eliminated. Cleavage can be detected by binding a pair of fluorescent adducts to the γ-cleaved βAPP fragment. Preferably, a first fluorescent adduct binds to the carboxy-terminal end of the γ-cleaved βAPP fragment, with substantially no cross-reactivity to uncleaved βAPP or to other types of γ-cleaved βAPP fragments, while a second fluorescent adduct binds to a portion within the amino-terminal region on the γ-cleaved βAPP fragment. Detection of binding to the γ-cleaved βAPP fragment is determined by monitoring the fluorescent energy transfer between the adducts.

IT 76555-98-1

RL: NUU (Other use, unclassified); USES (Uses)

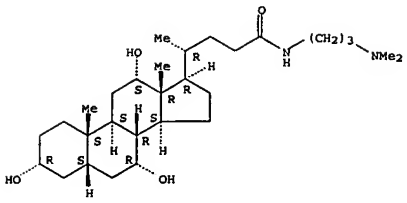
(solubilizer; isolation of functionally active γ-secretase presenilin 1 complex and fluorescence assay for γ-secretase activity and inhibitors)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L15 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



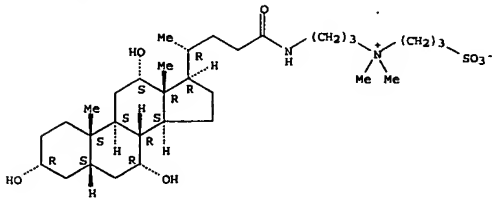
L15 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
1996:367800 Document No. 125:31908 Buffer system for increasing seroconversion efficiency. Smith, Daniel S.; Walker, John C. (Curators of the University of Missouri, USA). PCT Int. Appl. WO 9607318 A1 19960314, 72 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US11462 19950907. PRIORITY: US 1994-303156 19940908.

AB A method of increasing efficiency of deantigenation of blood group epitopes on erythrocytes (seroconversion) by exoglycosidases utilizing a step of performing the deantigenation in a zwitterionic buffer. The method provides a buffer system and exoglycosidase that utilized a twenty to one hundred fold lower total enzyme mass than the prior art methods. Zwitterions are selected from glycine, alanine, CHAPS, etc., and exoglycosidases are selected from Glycine max α-D-galactosidase, Gallus domesticus α-N-acetylgalactosaminidase, Phaseolus vulgaris α-N-acetyl-galactosidase and other multimeric eucaryotic exoglycosidases.

IT 75621-03-3, CHAPS
RL: MOA (Modifier or additive use); USES (Uses)
(zwitterion buffer and exoglycosidases for increasing efficiency of deantigenation of blood group epitopes on erythrocytes or seroconversion)

RN 75621-03-3 HCAPLUS
CN 1-Propanaminium, N,N-dimethyl-N-(3-sulfopropyl)-3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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           772898 GAMMA
             4935 GAMMAS
           773055 GAMMA
                  (GAMMA OR GAMMAS)
           320371 SECRET?
             2896 (G OR GAMMA)(W)SECRET?
          1724457 PROTEIN
          1196534 PROTEINS
          2002147 PROTEIN
                  (PROTEIN OR PROTEINS)
                7 COCMPLEX
                4 COCMPLEXES
               11 COCMPLEX
                  (COCMPLEX OR COCMPLEXES)
                0 PROTEIN COCMPLEX
                  (PROTEIN(W)COCMPLEX)
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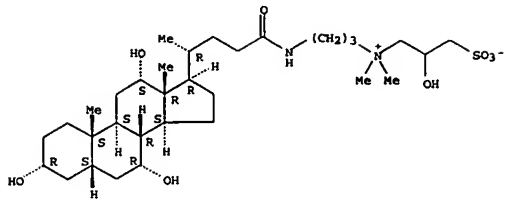
Searched by: Mary Hale 571-272-2507 REM 1D86

L19 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
2004:552244 Document No. 141:238713 Purification and Characterization of the
Human γ -Secretase Complex. Fraering, Patrick C.; Ye, Wenjuan; Strub, Jean-Marc; Dolios, Georgia; LaVoie, Matthew J.; Ostaszewski, Beth L.; van Dorsselaer, Alain; Wang, Rong; Selkoe, Dennis J.; Wolfe, Michael S. (Center for Neurologic Diseases, Brigham and Women's
Hospital and Harvard Medical School, Boston, MA, 02115, USA). Biochemistry, 43(30), 9774-9789 (English) 2004. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.
AB γ -Secretase is a member of an unusual class of proteases with intramembrane catalytic sites. This enzyme cleaves many type I membrane proteins, including the amyloid β-protein (Aβ) precursor (APP) and the Notch receptor. Biochem. and genetic studies have
identified four membrane proteins as components of γ -secretase: heterodimeric presenilin (PS) composed of its N- and C-terminal fragments (PS-NTF/CTF), a mature glycosylated form of nicastrin
(NCT), Aph-1, and Pen-2. Recent data from studies in Drosophila, mammalian, and yeast cells suggest that PS, NCT, Aph-1, and Pen-2 are necessary and sufficient to reconstitute γ -secretase activity. However, many unresolved issues, in particular the possibility of other structural or regulatory components, would be resolved by actually purifying the enzyme. Here, we report a detailed, multistep purification procedure for active γ -secretase and an initial characterization of the purified protease. Extensive mass spectrometry of the purified proteins strongly suggests that PS-NTF/CTF, mNCT, Aph-1, and Pen-2 are the components of active γ -secretase. Using the purified . gamma.-secretase, we describe factors that modulate the production of specific Aβ species: (1) phosphatidylcholine and sphingomyelin dramatically improve activity without changing cleavage specificity within an APP substrate; (2) increasing CHAPSO concns. from 0.1 to 0.25% yields a .apprx.100% increase in Aβ42 production; (3) exposure of an APP-based recombinant substrate to 0.5% SDS modulates cleavage specificity from a disease-mimicking pattern (high Aβ42/43) to a physiol. pattern (high Aβ40); and (4) sulindac sulfide directly and preferentially decreases Aβ42 cleavage within the purified complex. Taken together, our results define a procedure for purifying active γ -secretase and suggest that the lipid-mediated conformation of both enzyme and substrate regulate the production of the potentially neurotoxic Aβ42 and Aβ43 peptides.
IT 82473-24-3, CHAPSO
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CHAPSO and sodium dodecyl sulfate promotes amyloid β-protein precursor cleavage)
RN 82473-24-3 HCAPLUS
CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

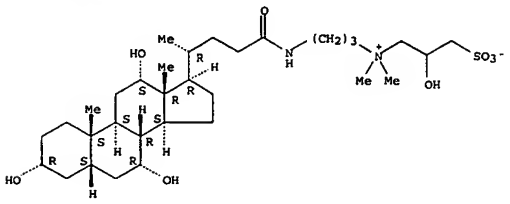
Absolute stereochemistry.

L19 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



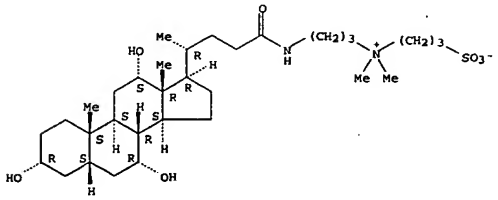
L19 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
2004:504793 Document No. 141:50129 Assay for gamma secretase modulators. Beher, Dirk (Merck Sharp & Dohme Limited, UK). Brit. UK Pat. Appl. GB 2396415 A1 20040623, 30 pp. (English). CODEN: BAXXDU. APPLICATION: GB 2003-28875 20031212. PRIORITY: GB 2002-29582 20021219.
AB An assay for identifying compds. that interact with the γ -secretase complex comprising preparing and solubilizing a source of the complex, incubating a test compound together with an affinity probe and
the source, capturing the resulting bound complex, and analyzing the components of the complex to determine whether the test compound has interacted
with the complex by determining the amount of PS1-NTF, PS1-CTF or mature nicastrin
present in the complex. The assay may be used in the identification of components of the γ -secretase complex.
IT 82473-24-3, CHAPSO
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(assay for gamma secretase modulators)
RN 82473-24-3 HCAPLUS
CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
2003:173459 Document No. 138:217451 Preparation, substrate specificity, and therapeutic uses of human γ3 protease involved in processing of amyloid precursor protein. Crouthamel, Ming-Chih; Gardell, Stephen J.; Huang, Qian; Lai, Ming-Tain; Li, Yueming (Merck & Co., Inc., USA). PCT Int. Appl. WO 2003018050 A1 20030306, 48 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US26969 20020808. PRIORITY: US 2001-PV311410 20010810.
AB The invention provides γ3 protease, a novel aspartyl class protease that is capable of taking part in the processing of amyloid precursor protein (APP) to Aβ peptide. The γ3 protease may be involved in the development and/or progression of Alzheimer's disease. It has a Mr
of 60-120 kDa on gel filtration, and its activity is inhibited by pepstatin A but not by L685,458 (a known γ -secretase inhibitor) with a pH optimum of 6.0. γ3 Protease cleaves amyloid precursor protein, as well as artificial substrates incorporating portions of APP695, at the same or similar sites as . gamma.-secretase, but can be distinguished from the known γ -secretase activity involving presenilin-1 and presenilin-2. Methods of assaying γ3 protease and identifying potential inhibitors, useful in the prevention or treatment of
Alzheimer s disease, are disclosed.
IT 75621-03-3, CHAPS 82473-24-3, CHAPSO
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of γ3 protease from biol. membranes in presence of; preparation, substrate specificity, and therapeutic uses of human γ3 protease involved in processing of amyloid precursor protein)
RN 75621-03-3 HCAPLUS
CN 1-Propanaminium, N,N-dimethyl-N-(3-sulfopropyl)-3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-, inner salt (9CI) (CA INDEX NAME)

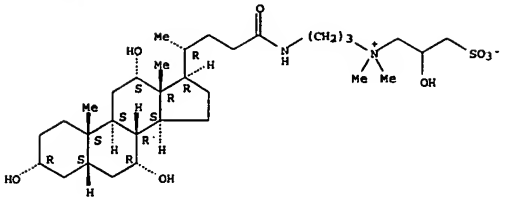
Absolute stereochemistry.



RN 82473-24-3 HCAPLUS
CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L19 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L19 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

2001:816967 Document No. 135:354682 γ -Secretase substrates and in vitro assays. Li, Yueming; Xu, Min; Huang, Qian; Gardell, Stephen (Merck & Co., Inc., USA). PCT Int. Appl. WO 2001083811 A1 20011108, 36 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US13332 20010425. PRIORITY: US 2000-PV201053 20000501.

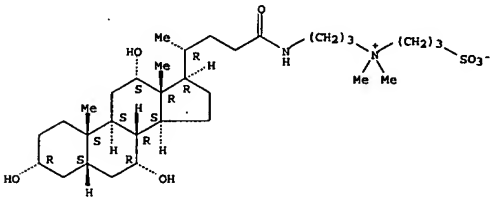
AB The present invention features γ -secretase substrates and in vitro assays for measuring γ -secretase activity employing such substrates. The .gamma.-secretase substrates described herein contain a hydrophilic polypeptide moiety (Asp-Tyr-Lys-Asp-Asp-Asp-Asp-Lys) covalently joined to the C-terminus of a β-CTP domain. A "β-CTF domain" is a polypeptide that can be cleaved by γ -secretase and which approximates the C-terminal fragment (amino acids 596-695) of human amyloid precursor protein (APP) produced after cleavage of APP by a β-secretase, or is a functional derivative thereof. The hydrophilic polypeptide is chosen to increase the solubility of the γ -secretase substrate in a zwitterionic detergent. Thus, a fusion protein consisting sequentially of an N-terminal Met, human APP(597-695), and the Flag tag sequence is processed by γ -secretase. The Aβ40 and Aβ42-related products are detected by electrochemiluminescence using biotinylated 4G8 antibody and ruthenylated G2-10 or FCA3542, resp.

IT 75621-03-3, CHAPS 82473-24-3, CHAPSO
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(zwitterionic detergent; γ -secretase substrates and in vitro assays)

RN 75621-03-3 HCAPLUS

CN 1-Propanaminium, N,N-dimethyl-N-(3-sulfopropyl)-3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

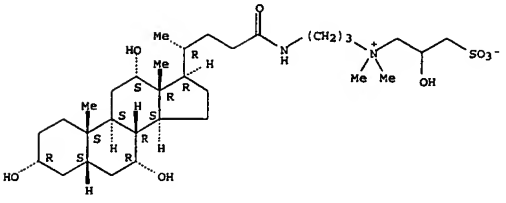


RN 82473-24-3 HCAPLUS

CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L19 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L19 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

2000:392881 Document No. 133:146729 Presenilin 1 is linked with .gamma.-secretase activity in the detergent solubilized state. Li, Yue-Ming; Lai, Ming-Tain; Xu, Min; Huang, Qian; DiMuzio-Mower, Jillian; Sardana, Mohinder K.; Shi, Xiao-Ping; Yin, Kuo-Chang; Shafer, Jules A.; Gardell, Stephen J. (Department of Biological Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA). Proceedings of the National Academy of Sciences of the United States of America, 97(11), 6138-6143 (English) 2000. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

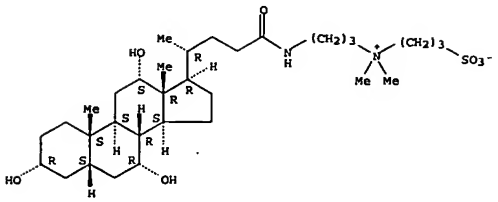
AB γ -Secretase is a membrane-associated protease that cleaves within the transmembrane region of amyloid precursor protein to generate the C termini of the two Aβ peptide isoforms, Aβ40 and Aβ42. Here we report the detergent solubilization and partial characterization of γ -secretase. The activity of solubilized γ -secretase was measured with a recombinant substrate, C100Flag, consisting largely of the C-terminal fragment of amyloid precursor protein downstream of the β-secretase cleavage site. Cleavage of C100Flag by γ -secretase was detected by electrochemiluminescence using antibodies that specifically recognize the Aβ40 or Aβ42 termini. Incubation of C100Flag with HeLa cell membranes or detergent-solubilized HeLa cell membranes generates both the Aβ40 and Aβ42 termini. Recovery of catalytically competent, soluble γ -secretase critically depends on the choice of detergent; CHAPSO (3-[(3-cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate) but not Triton X-100 is suitable. Solubilized γ -secretase activity is inhibited by pepstatin and more potently by a novel aspartyl protease transition-state analog inhibitor that blocks formation of Aβ40 and Aβ42 in mammalian cells. Upon gel exclusion chromatog., solubilized γ -secretase activity coelutes with presenilin 1 (PS1) at an apparent relative mol. weight of approx. 2.0 + 106. Anti-PS1 antibody immunoppts. .gamma.-secretase activity from the solubilized γ -secretase preparation These data suggest that γ -secretase activity is catalyzed by a PS1-containing macromol. complex.

IT 75621-03-3, CHAPS 82473-24-3, CHAPSO
RL: NUU (Other use, unclassified); USES (Uses)
(presenilin 1 is linked with γ -secretase activity in the detergent-solubilized state)

RN 75621-03-3 HCAPLUS

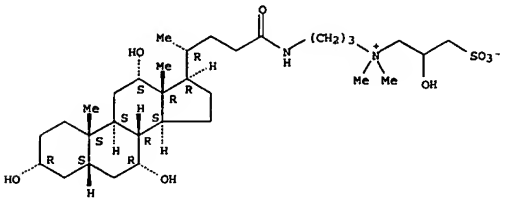
CN 1-Propanaminium, N,N-dimethyl-N-(3-sulfopropyl)-3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 82473-24-3 HCAPLUS
CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



```
=> s l8 and secretase
          1795 SECRETASE
           288 SECRETASES
          1852 SECRETASE
                 (SECRETASE OR SECRETASES)
L20          6 L8 AND SECRETASE

=> s l20 not (l19 or l15 or l16)
L21          0 L20 NOT (L19 OR L15 OR L16)

=> del his y

=> fil reg
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      54.22     305.05

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -5.84     -12.41

FILE 'REGISTRY' ENTERED AT 14:05:45 ON 22 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   20 MAR 2005  HIGHEST RN 845957-95-1
DICTIONARY FILE UPDATES:  20 MAR 2005  HIGHEST RN 845957-95-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
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Searched by: Mary Hale 571-272-2507 REM 1D86

```
=> d his ful

     FILE 'HCAPLUS' ENTERED AT 16:53:03 ON 18 MAR 2005
                  E ROBERTS SUSAN B/AU
L58            61 SEA ABB=ON  ("ROBERTS SUSAN B"/AU OR "ROBERTS SUSAN BOSEMAN"/AU
                  )
                  E HENDRICK JOSEPH P/AU
L59            23 SEA ABB=ON  ("HENDRICK JOSEPH"/AU OR "HENDRICK JOSEPH P"/AU OR
                  "HENDRICK JOSEPH P JR"/AU OR "HENDRICK JOSEPH PATRICK"/AU)
                  E VINITSKY ALEXANDER/AU
L60            20 SEA ABB=ON  ("VINITSKY A"/AU OR "VINITSKY A H"/AU OR "VINITSKY
                  ALEXANDER"/AU)
                  E LEWIS MARTIN A/AU
L61             6 SEA ABB=ON  "LEWIS MARTIN A"/AU
                  E SMITH DAVID W/AU
L62           179 SEA ABB=ON  ("SMITH DAVID W"/AU OR "SMITH DAVID W E"/AU OR
                  "SMITH DAVID WALLACE"/AU OR "SMITH DAVID WALTER"/AU OR "SMITH
                  DAVID WARREN"/AU OR "SMITH DAVID WAYNE"/AU)
                  E PAK ROGER HOCHOON/AU
L63            10 SEA ABB=ON  ("PAK ROGER"/AU OR "PAK ROGER H"/AU OR "PAK ROGER
                  HOCHOON"/AU)
L64           292 SEA ABB=ON  L58 OR L59 OR L60 OR L61 OR L62 OR L63
L65             0 SEA ABB=ON  L58 AND L58 AND L60 AND L61 AND L62 AND L63
L66             7 SEA ABB=ON  L64 AND ?GAMMA?(W)?SECRETASE?
L67             1 SEA ABB=ON  L66 AND ?ISOLATION?
                  SELECT RN L67 1-1

     FILE 'REGISTRY' ENTERED AT 16:55:43 ON 18 MAR 2005
L68            27 SEA ABB=ON  (338454-52-7/BI OR 146368-14-1/BI OR 146368-16-3/BI
                   OR 199164-91-5/BI OR 2321-07-5/BI OR 247144-99-6/BI OR
                  262412-30-6/BI OR 264902-77-4/BI OR 304014-12-8/BI OR 366488-00
                  -8/BI OR 366488-01-9/BI OR 366520-85-6/BI OR 366520-86-7/BI OR
                  366522-28-3/BI OR 366522-29-4/BI OR 366801-12-9/BI OR 366801-14
                  -1/BI OR 50402-56-7/BI OR 6268-49-1/BI OR 70281-37-7/BI OR
                  7440-33-7/BI OR 7440-53-1/BI OR 7440-63-3/BI OR 76555-98-1/BI
                  OR 7782-39-0/BI OR 81-88-9/BI OR 91-64-5/BI)

     FILE 'HCAPLUS' ENTERED AT 16:55:52 ON 18 MAR 2005
L69             1 SEA ABB=ON  L67 AND L68

     FILE 'REGISTRY' ENTERED AT 17:00:18 ON 18 MAR 2005
                  E CHAPSO/CN
                  E MCHAPSO/CN
L70             1 SEA ABB=ON  CHAPSO/CN

     FILE 'HCAPLUS' ENTERED AT 17:02:24 ON 18 MAR 2005
L71             0 SEA ABB=ON  MCHAPSO
L72             0 SEA ABB=ON  ?MCHAPSO?

     FILE 'REGISTRY' ENTERED AT 17:03:41 ON 18 MAR 2005
                  E N-3DIMETHYLAMINOPROPYL/CN
                  E N-3-DIMETHYLAMINOPROPYL/CN
                  E CHOLAN-2-AMIDE/CN
                  E CHOLANE/CN
L73             1 SEA ABB=ON  CHOLANE/CN
                  E CHOLAN-2-AMIDE/CN
                  E CHOLANAMIDE/CN
L74             1 SEA ABB=ON  CHOLANAMIDE/CN
L75               STRUCTURE 26665-96-3
L76             0 SEA SSS SAM L75
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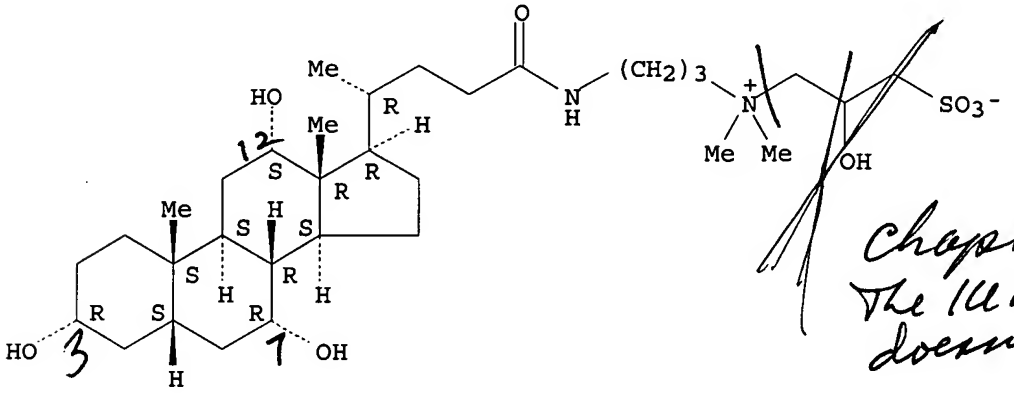
Inventor search

L77 12 SEA SSS FUL L75
L78 1 SEA ABB=ON 76555-98-1/RN See attachment (8)

FILE 'HCAPLUS' ENTERED AT 17:27:09 ON 18 MAR 2005
L79 7 SEA ABB=ON L78 7 hits from CA Plus

L70 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 82473-24-3 REGISTRY
CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cholane, 1-propanaminium deriv.
OTHER NAMES:
CN 3-[(3-Cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate
CN **CHAPSO**
FS STEREOSEARCH
DR 120893-60-9
MF C32 H58 N2 O8 S
LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, MRCK*, MSDS-OHS, PIRA, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



Chapso has sulfonate; The IUPAC name given doesn't include sulfonate

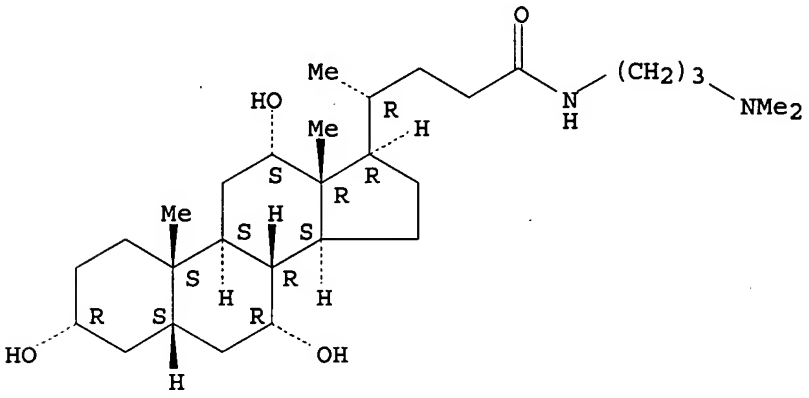
185 REFERENCES IN FILE CA (1907 TO DATE)
185 REFERENCES IN FILE CAPLUS (1907 TO DATE)
ED Entered STN: 16 Nov 1984

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE TOTAL

=> d

L78 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN **76555-98-1** REGISTRY
CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H52 N2 O4
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: USES (Uses)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)
ED Entered STN: 16 Nov 1984

This structure matches the IUPAC name given.

=> d ibib abs hitstr l69 1-1

L69 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:748108 HCAPLUS
DOCUMENT NUMBER: 135:300482
TITLE: **Isolation** of functionally active . **gamma.-secretase** presenilin 1 complex and fluorescence assay for γ - **secretase** activity and inhibitors
INVENTOR(S): **Roberts, Susan B.; Hendrick, Joseph P.; Vinitsky, Alexander;** Lewis, Martin; **Smith, David W.; Pak, Roger**
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001075435	A2	20011011	WO 2001-US10453	20010330
WO 2001075435	A3	20020808		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2405332	AA	20011011	CA 2001-2405332	20010330
US 2002025540	A1	20020228	US 2001-823153	20010330
US 6713248	B2	20040330		
EP 1305634	A2	20030502	EP 2001-922976	20010330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004505608	T2	20040226	JP 2001-572863	20010330
US 2004121411	A1	20040624	US 2003-713981	20031114

PRIORITY APPLN. INFO.:

US 2000-194495P	P	20000403
US 2001-823153	A3	20010330
WO 2001-US10453	W	20010330

AB The present invention provides an isolated, functionally-active protein that catalyzes cleavage of a γ -**secretase** substrate. The functional activity of the isolated protein suggests that the isolated protein includes γ -**secretase.** In one embodiment, the isolated γ -**secretase** protein is associated with presenilin 1. The present invention also relates to homogeneous methods for monitoring cleavage of β-amyloid precursor protein (βAPP) by γ -**secretase**, wherein the steps of isolating and retrieving cleavage products have been eliminated. Cleavage can be detected by binding a pair of fluorescent adducts to the γ-cleaved βAPP fragment. Preferably, a first fluorescent adduct binds to the carboxy-terminal end of the γ-cleaved βAPP fragment, with substantially no cross-reactivity to uncleaved βAPP or to other types of γ-cleaved βAPP fragments, while a second fluorescent adduct binds to a portion within the amino-terminal region on the γ-cleaved βAPP fragment. Detection of binding to the

γ-cleaved βAPP fragment is determined by monitoring the fluorescent energy transfer between the adducts.

IT **366522-28-3**
RL: PRP (Properties)
(Unclaimed; **isolation** of functionally active γ **-secretase** presenilin 1 complex and fluorescence assay for γ **-secretase** activity and inhibitors)
RN 366522-28-3 HCAPLUS
CN 24: PN: WO0175435 SEQID: 7 unclaimed protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **262412-30-6P 366520-86-7P**
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; **isolation** of functionally active γ **-secretase** presenilin 1 complex and fluorescence assay for γ **-secretase** activity and inhibitors)
RN 262412-30-6 HCAPLUS
CN Amyloid precursor protein (synthetic human C-terminal fragment 100-amino acid precursor) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 366520-86-7 HCAPLUS
CN Amyloid precursor protein (synthetic human isoform C-83) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **7440-33-7**, Tungsten, analysis **7782-39-0**, Deuterium, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(deuterium-tungsten lamp; **isolation** of functionally active γ **-secretase** presenilin 1 complex and fluorescence assay for γ **-secretase** activity and inhibitors)
RN 7440-33-7 HCAPLUS
CN Tungsten (8CI, 9CI) (CA INDEX NAME)

W

RN 7782-39-0 HCAPLUS
CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D—D

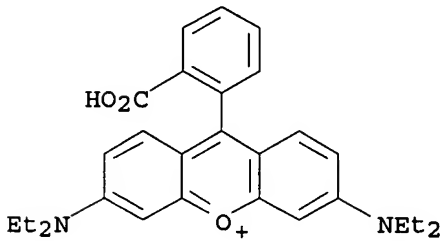
IT **7440-63-3**, Xenon, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(flash lamp; **isolation** of functionally active γ **-secretase** presenilin 1 complex and fluorescence assay for γ **-secretase** activity and inhibitors)
RN 7440-63-3 HCAPLUS
CN Xenon (8CI, 9CI) (CA INDEX NAME)

Xe

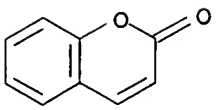
IT **338454-52-7DP**, γ -**Secretase**, complexes
with presenilin 1
RL: ANT (Analyte); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**isolation** of functionally active γ -**secretase** presenilin 1 complex and fluorescence assay for γ -**secretase** activity and inhibitors)
RN 338454-52-7 HCAPLUS
CN γ-Secretase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **338454-52-7**, γ -**Secretase**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**isolation** of functionally active γ -**secretase** presenilin 1 complex and fluorescence assay for γ -**secretase** activity and inhibitors)
RN 338454-52-7 HCAPLUS
CN γ-Secretase (9CI) (CA INDEX NAME)

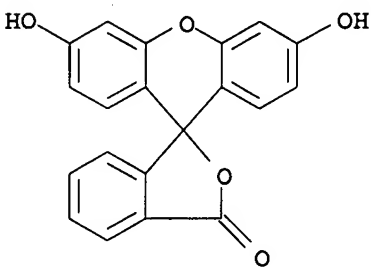
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **81-88-9 91-64-5**, Coumarin **2321-07-5**,
Fluorescein **6268-49-1 7440-53-1D**, Europium, cryptates,
biological studies **50402-56-7**, EDANS **70281-37-7**,
Tetramethylrhodamine **146368-14-1 146368-16-3**
247144-99-6 304014-12-8D, salts
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**isolation** of functionally active γ -**secretase** presenilin 1 complex and fluorescence assay for γ -**secretase** activity and inhibitors)
RN 81-88-9 HCAPLUS
CN Xanthylium, 9-(2-carboxyphenyl)-3,6-bis(diethylamino)-, chloride (9CI) (CA INDEX NAME)



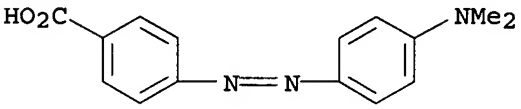
RN 91-64-5 HCAPLUS
CN 2H-1-Benzopyran-2-one (9CI) (CA INDEX NAME)



RN 2321-07-5 HCAPLUS
CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 3',6'-dihydroxy- (9CI) (CA INDEX NAME)



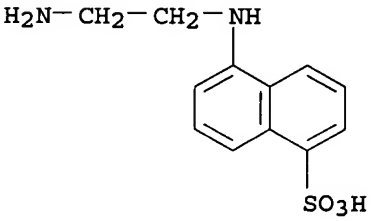
RN 6268-49-1 HCAPLUS
CN Benzoic acid, 4-[[4-(dimethylamino)phenyl]azo]- (9CI) (CA INDEX NAME)



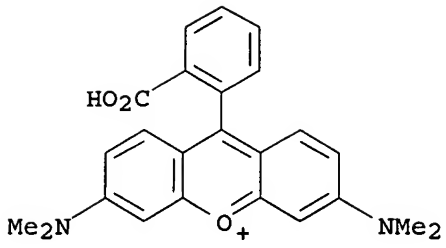
RN 7440-53-1 HCAPLUS
CN Europium (8CI, 9CI) (CA INDEX NAME)

Eu

RN 50402-56-7 HCAPLUS
CN 1-Naphthalenesulfonic acid, 5-[(2-aminoethyl)amino]- (9CI) (CA INDEX NAME)

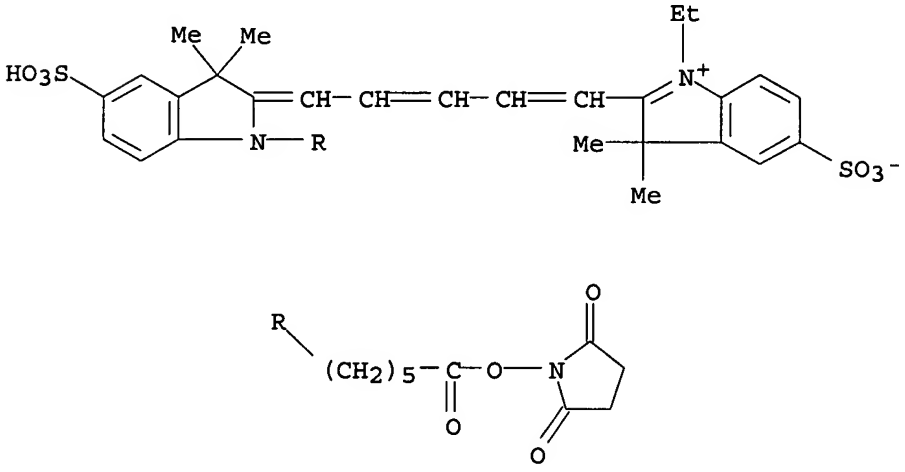


RN 70281-37-7 HCAPLUS
CN Xanthylium, 9-(2-carboxyphenyl)-3,6-bis(dimethylamino)-, chloride (9CI) (CA INDEX NAME)

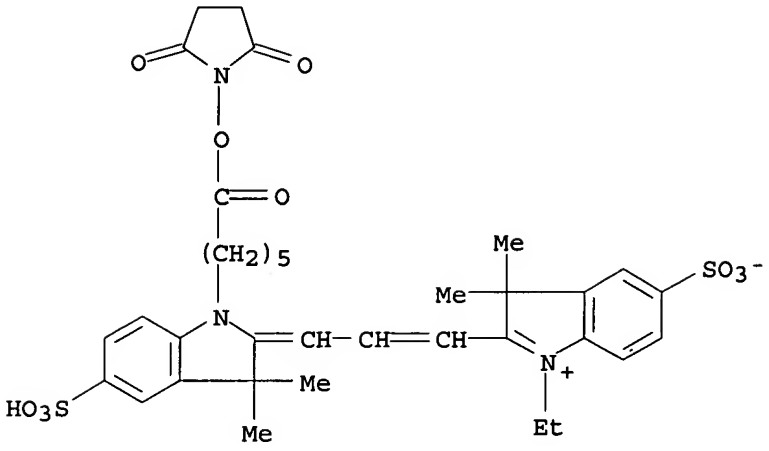


● Cl^-

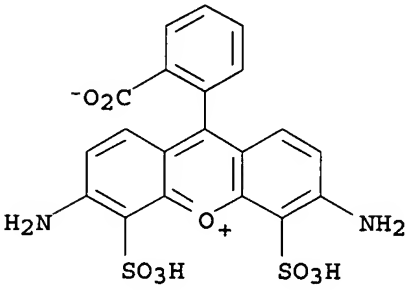
RN 146368-14-1 HCAPLUS
CN 3H-Indolium, 2-[5-[1-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene]-1,3-pentadienyl]-1-ethyl-3,3-dimethyl-5-sulfo-, inner salt (9CI) (CA INDEX NAME)



RN 146368-16-3 HCAPLUS
CN 3H-Indolium, 2-[3-[1-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene]-1-propenyl]-1-ethyl-3,3-dimethyl-5-sulfo-, inner salt (9CI) (CA INDEX NAME)



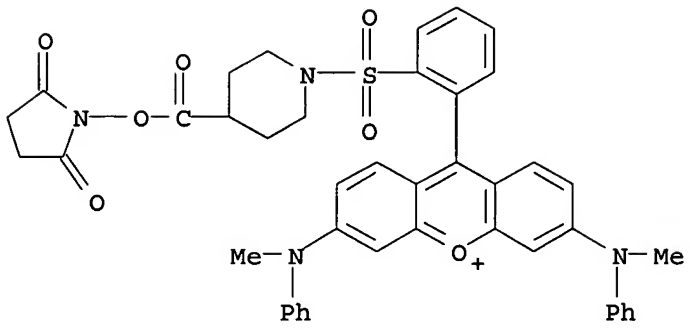
RN 247144-99-6 HCAPLUS
CN Xanthylium, 3,6-diamino-9-[2,4(or 2,5)-dicarboxyphenyl]-4,5-disulfo-, inner salt, trilithium salt (9CI) (CA INDEX NAME)



D1— CO_2H

●3 Li

RN 304014-12-8 HCAPLUS
CN Xanthylium, 9-[2-[[4-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-1-piperidinyl]sulfonyl]phenyl]-3,6-bis(methylphenylamino)-, chloride (9CI) (CA INDEX NAME)



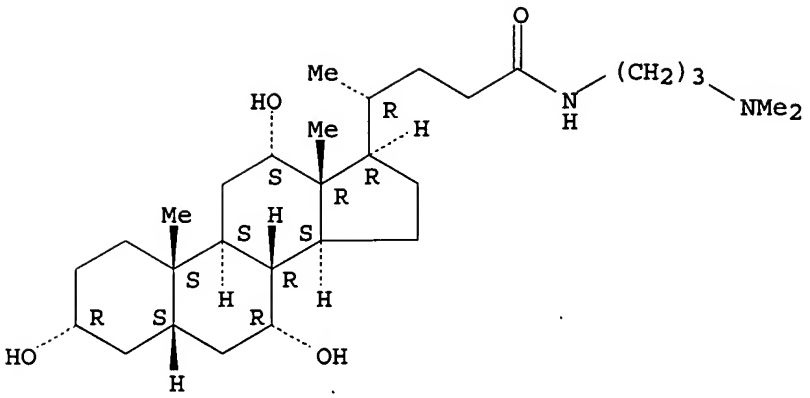
● Cl⁻

IT **264902-77-4P**, 3: PN: DE19849073 SEQID: 3 unclaimed DNA
366520-85-6P
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; **isolation** of functionally active γ **-secretase** presenilin 1 complex and fluorescence assay for γ **-secretase** activity and inhibitors)
RN 264902-77-4 HCAPLUS
CN 3: PN: DE19849073 SEQID: 3 unclaimed DNA (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 366520-85-6 HCAPLUS
CN DNA (synthetic human amyloid precursor protein isoform C-83-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **76555-98-1**
RL: NUU (Other use, unclassified); USES (Uses)
(solubilizer; **isolation** of functionally active γ **-secretase** presenilin 1 complex and fluorescence assay for γ **-secretase** activity and inhibitors)
RN 76555-98-1 HCAPLUS
CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **366522-29-4 366801-12-9 366801-14-1**
RL: PRP (Properties)
(unclaimed protein sequence; **isolation** of functionally active γ -**secretase** presenilin 1 complex and fluorescence assay for γ -**secretase** activity and inhibitors)
RN 366522-29-4 HCAPLUS
CN 7: PN: WO0175435 SEQID: 8 unclaimed protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 366801-12-9 HCAPLUS
CN 9: PN: WO0175435 SEQID: 10 unclaimed protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 366801-14-1 HCAPLUS
CN 10: PN: WO0175435 SEQID: 11 unclaimed protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **199164-91-5 366488-00-8 366488-01-9**
RL: PRP (Properties)
(unclaimed sequence; **isolation** of functionally active γ -**secretase** presenilin 1 complex and fluorescence assay for γ -**secretase** activity and inhibitors)
RN 199164-91-5 HCAPLUS
CN L-Arginine, L-cysteinyl-L-arginyl-L-α-aspartyl-L-seryl-L-histidyl-L-leucylglycyl-L-prolyl-L-histidyl-L-arginyl-L-seryl-L-threonyl-L-prolyl-L-α-glutamyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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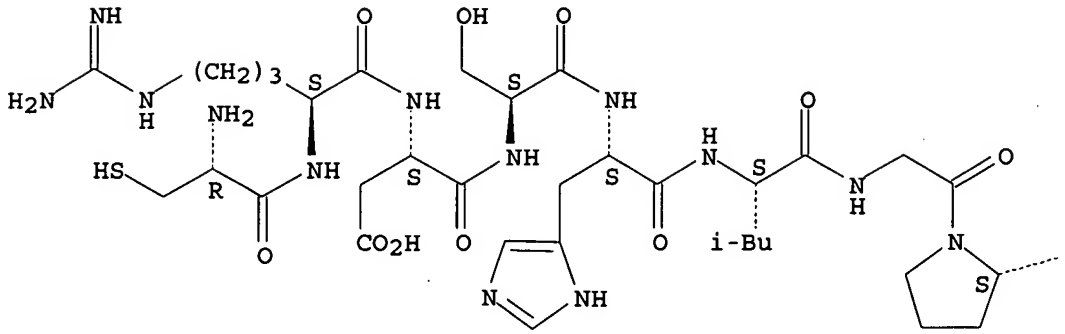

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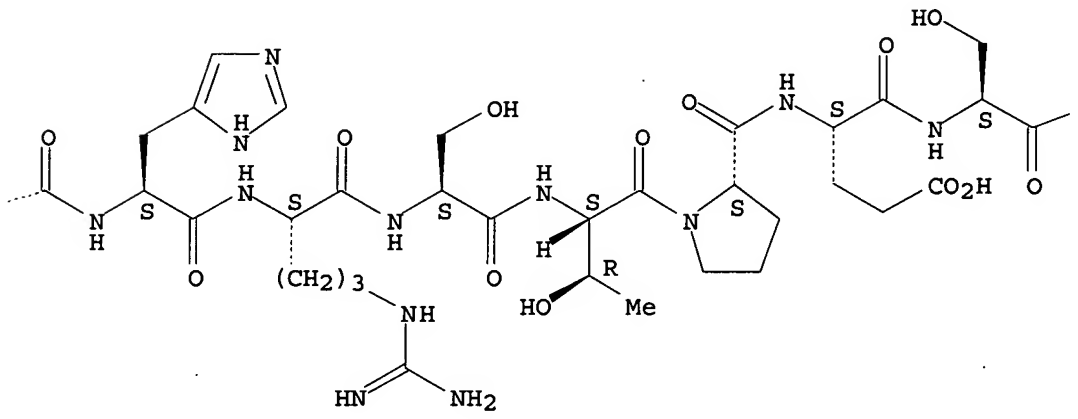

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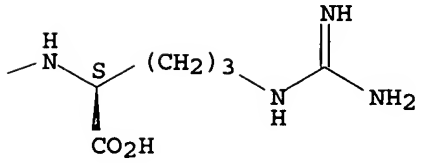

RN 366488-00-8 HCAPLUS
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Absolute stereochemistry.

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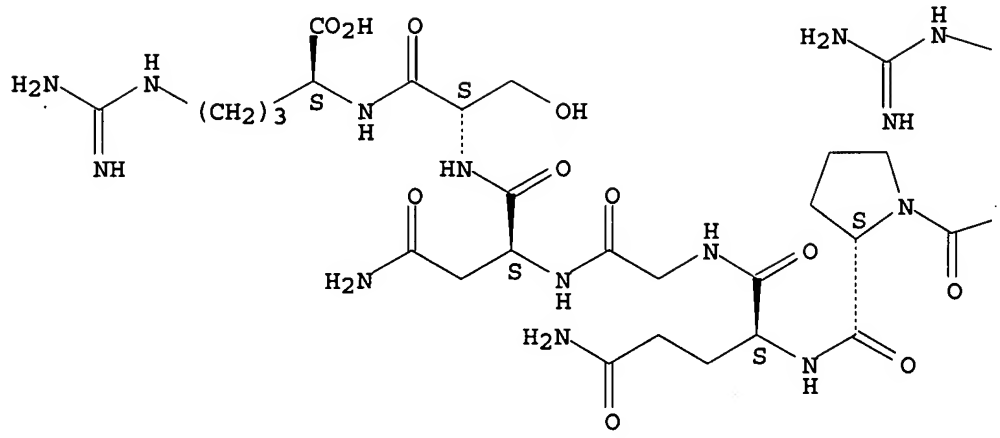

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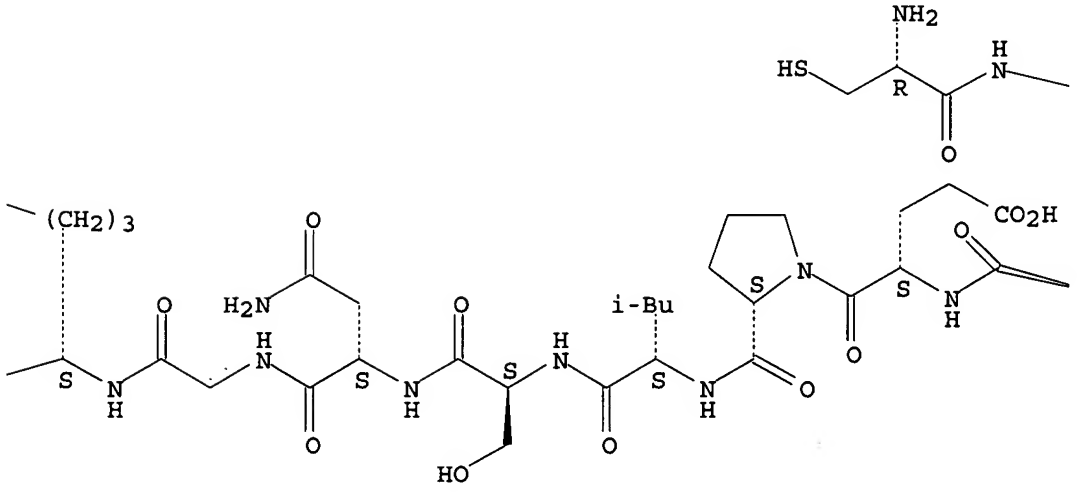

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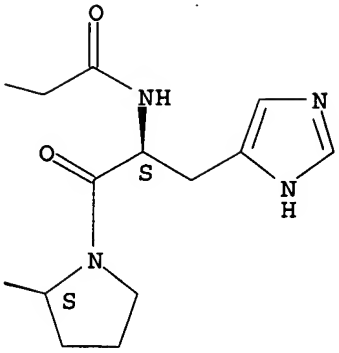

RN 366488-01-9 HCAPLUS
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Absolute stereochemistry.

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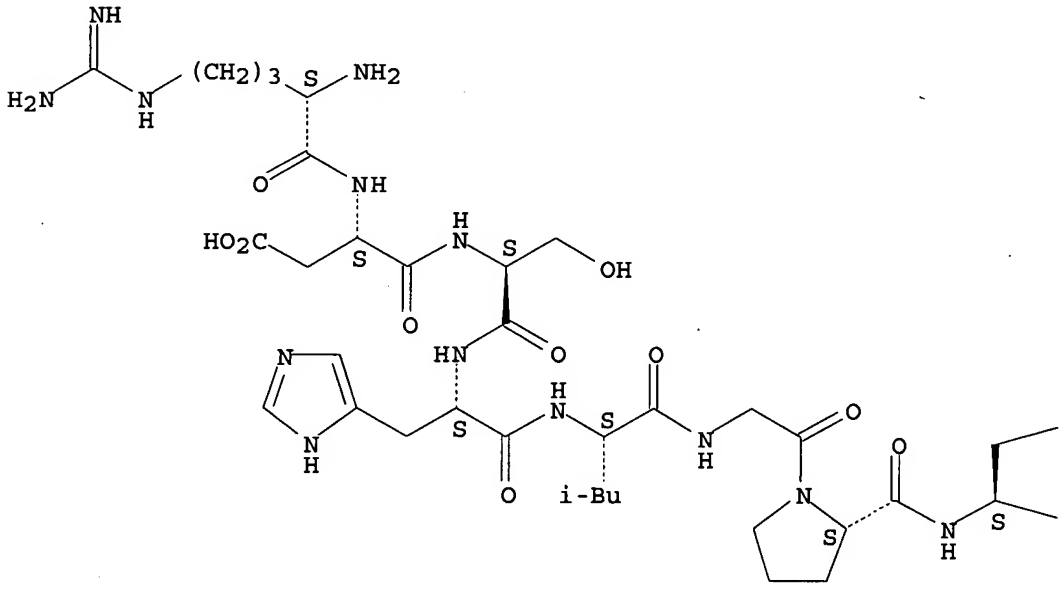

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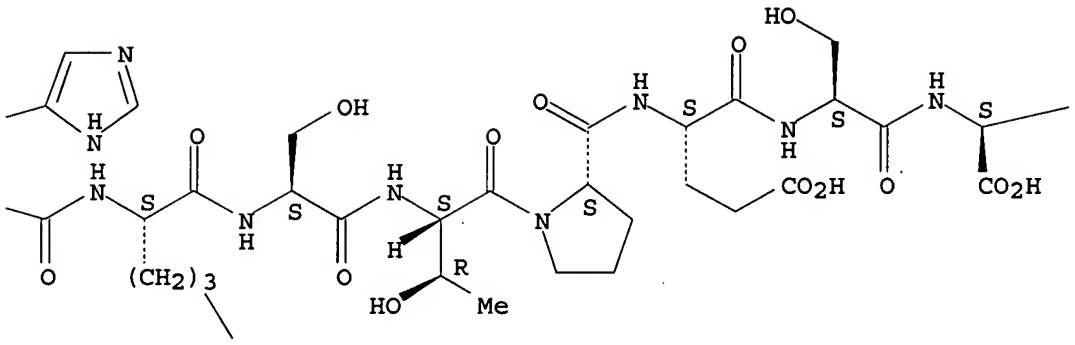

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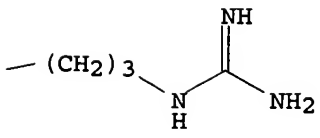

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